Combinatorial Materials Science: The Scylla Chemical Approach.

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Combinatorial Materials Science

- **Library Synthesis**
  - Homogeneous & Heterogeneous Catalysis
  - Electronic & Optical Materials
- **Library Screening**
  - Optical & Imaging Systems
  - Spectroscopic Analysis Techniques
- **Library Analysis**
  - Current Techniques (HT-MS, NMR, FT-IR)
  - New & Emerging Technologies

Scylla Chemical - Research Areas

- Pharmaceuticals
- Agrochemicals
- Catalysts
  - Homogeneous
  - Heterogeneous
- Polymers
  - Commodity
  - Specialty
- Pigments & Dyes
- Materials
  - Electronics
  - Smart Materials
  - Biomaterials
  - Optical
  - Glasses
  - Structural
- Specialty & Fine Chemicals
- Coatings

Scylla Chemical - R&D Capabilities

- Synthetic Chemistry
  - Organic
  - Inorganic
  - Organometallic
- High-Throughput Synthesis & Screening
- Process Chemistry
- Computational
- Analytical

- Engineering
  - Mechanical
  - Electrical
  - Chemical
  - Mechtronic/Robotics
  - Industrial/Controls
- Informatics
  - Control Systems
  - Systems Integration
  - dB Systems

Synthesis Technologies - Overview

- **Homogeneous Synthesis**
  - Solution-Phase Synthesis
  - Novel Liquid Phase Technologies
- **Heterogeneous Synthesis**
  - Solid-Phase Synthesis
  - Solids, Sol-Gel, Emulsions, Slurries
- **Process-Scale Synthesis**
  - Process Scale-Up
  - Biocatalysis Systems

Synthesis Technologies - Homogeneous

- **Small (Nano) Scale**
  - "Lab-on-a-Chip" Technologies
  - Integrated Circuits - Synthesis/Screen/Analysis
- **Medium (Milli/Micro) Scale**
  - Current State-of-the-Art Technologies
  - New Robotics and Control Systems
- **Large (g/kg) Scale**
  - Modular Components (same as Medium Scale)
  - Advanced Process Control Systems

Synthesis Technologies - Heterogeneous

- **Small (Nano) Scale**
  - "Lab-on-a-Chip" Technologies
  - Integrated Circuits - Synthesis/Screen/Analysis
  - Ink Jet, Nanofluidics, CVD, PVD, etc.
  - Solids Handling (e.g. Sol-Gel)
- **Medium & Large Scale**
  - Modular Components for Reaction Scaling
  - Process Mimicking Systems
  - Composition & Constitution Diversity Elements
  - Reaction Processing Technologies

Synthesis Technologies - Process-Scale

- **Scale-Up for:**
  - Advanced Properties Testing
  - Generating Customer Samples
- **High-Throughput Arrays**
  - Reactor Design & Control
  - Reaction Processing
- **All Synthesis Techniques**
  - Homogeneous, Heterogeneous & Biological
  - Building Blocks, Intermediates, Reagents, etc.

Screening Technologies - Overview

- Imaging Technologies
  - IR, NIR, UV-Vis, X-Ray, etc.
- Reactive Reagents
  - Dyes, Stains, Indicators, & Probes
- Spectroscopic Technologies
  - NMR, LCMS, ATR-FTIR, Fluorescence, etc.
- Surface & Sub-Surface Technologies
  - SEM, TEM, X-Ray, ATR, etc.
- Other Technologies
  - Electrochemical, Electrical, Electromagnetic, etc.

Screening Technologies - Homogeneous

- **Imaging Technologies**
  - Integrated with Synthesis Arrays
  - IR Thermography for Activity (Primary Level)
- **Reactive Reagents**
  - Introduction of Reactive Dyes to Screen Solution
  - Secondary Level Screen for Selectivity/Specificity
- **Spectroscopic Technologies**
  - Reduce Magnitude of Materials to Screen
  - Tertiary Level Screen for Advanced Properties

Screening Technologies - Heterogeneous

- **Imaging Technologies**
  - Integrated with Screening/Analysis System
  - IR Thermography for Activity (Primary Level)
- **Spectroscopic Technologies**
  - Integrated with Primary Screen System
  - Secondary Level Screen for Selectivity/Specificity
- **Surface & Subsurface Technologies**
  - Reduce Magnitude of Materials to Screen
  - Tertiary Level Screen for Advanced Properties

Screening Technologies - Advanced Technologies

- **Hybrid Systems**
  - Synthesis & Screening
  - Screening & Analysis
  - Synthesis, Screening & Analysis
- **Miniaturization (Nano-Scale)**
  - “Lab-on-a-Chip”
  - MEM’s - Micro-Machining
  - IC’s - Reactors, Reaction Control

Analytical Technologies - Overview

- **Current Technologies**
  - Classic Analytical/Properties Testing
  - Systems Integration with Automation Technologies
  - High-Throughput Operations
- **Next Generation Technologies**
  - Systems Design for High-Throughput
  - New Commercial Systems
  - Hybrid Analysis Systems

Analytical Technologies - General Properties

- **Chemical (Materials) Composition Analysis**
  - NMR, LC-NMR, HT-NMR (Multiple Nuclei)
  - FT-IR, NIR (Raman), ATR Microscopy
  - MS, LCMS, LCMS/MS, GCMS, HT-MS
    - EI, CI, ESI, APCI, FAB, MALDI, TOF, etc.
  - UV/Vis, Fluorescence, Phosphorescence
  - Surface Analysis Techniques
    - XRD, XRF, XRA, SEM, TEM, etc.
  - Other Techniques
    - AA, Elemental Analysis, Chromatography

Analytical Technologies - Advanced Properties

- **Chemical (Materials) Properties Analysis**
  - Mechanical Properties
  - Thermal Properties
  - Electrical Properties
  - Optical Properties
  - Electromagnetic/Magnetic Properties
  - Mass Properties (MW, Morphology)
  - Surface Appearance Properties
  - Environmental Properties

Computational Technologies - Overview

- Planning & Tracking
  - Integrated Electronic Notebook
    - Coupled to Process Control System
  - “Cradle to Grave” Tracking
    - Inventory to Archival
- Predictive Tools
  - Integrated dB System
    - COSMOS™
  - Intelligent Systems
    - Neutral Networks, Fuzzy Logic

Computational Technologies - Planning & Tracking

- **Planning & Tracking**
  - Integrated dB System
  - Inventory/Ordering Tracking
  - Synthesis Planning/Registration
  - Integrated with Process Control
  - Individual Materials Biography for Intellectual Property Management
  - GUI for Query/Search
  - Screening & Analysis Data

Computational Technologies - Predictive Tools

- **Predictive Tools**
  - Integrated dB System
  - Diversity Analysis - Multiple Properties
  - QSAR/QSPR - Feedback Mechanisms
  - MVPO Reaction Optimization Strategies
  - Automated Analytical Data Verification
  - Process Validation - Quantitative Process/Scale Relationships (to validate miniaturization)
  - Advanced Modelling Technologies

Model Study - Project Overview

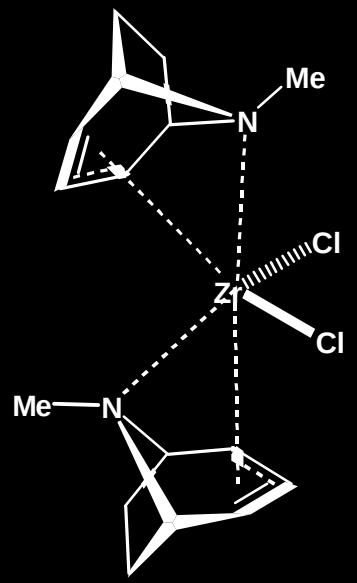
- **CMS Research Program**
  - Reaction Type: Homogeneous Catalysis
    - Ethylene Polymerization
  - High-Throughput Chemical Synthesis
    - Ligand Libraries
    - Metallocene Complexes (Group IV Transition Metals)
  - High-Throughput Chemical Screening
    - General Reactivity and Stability
    - Detailed Kinetics and Product Properties

Model Study - Project Overview

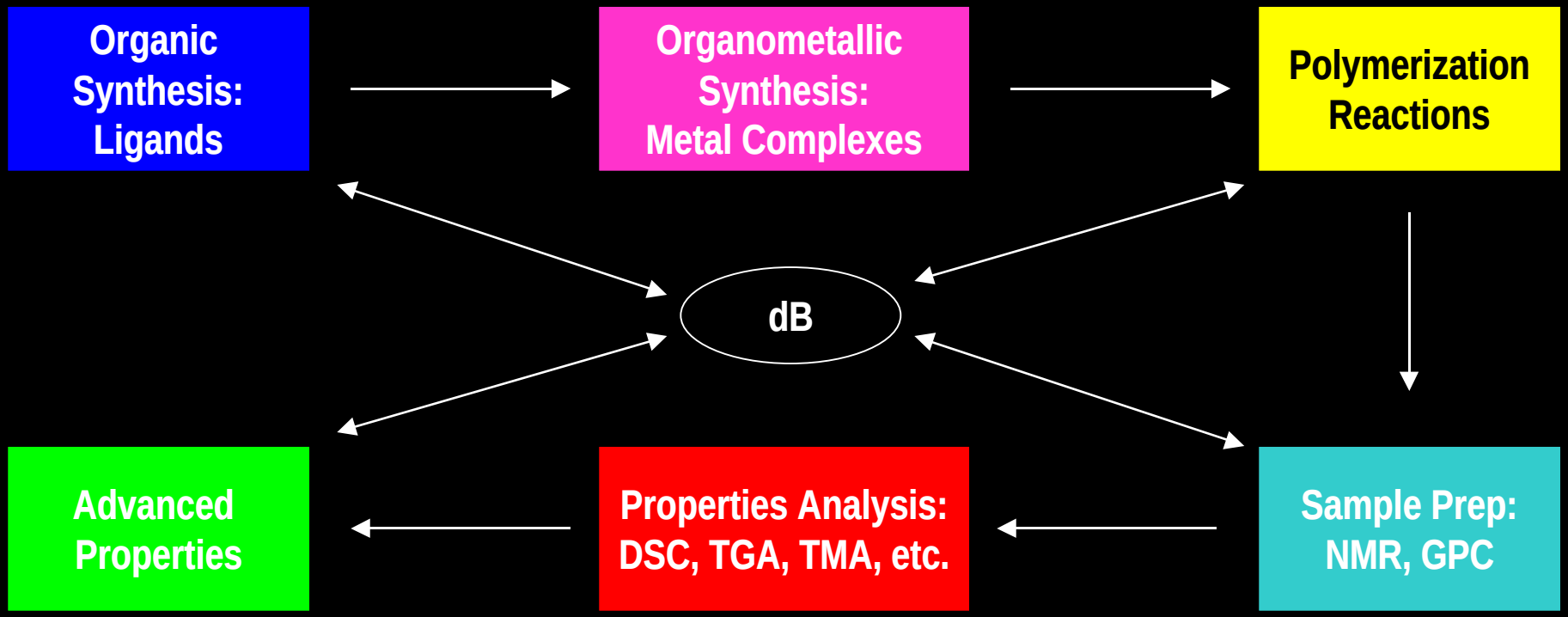
- **Catalyst Hypothesis**
  - Proposal to Design Libraries of Metallocene's Derived from Bergman's Tropidinyl Ligands.
  - Ligands will be used to assemble Group IV complexes.
  - Complexes tested for ability to catalyze Ethylene Polymerization.

Bergman, R.G., et. al.
Angew. Chem. Int. Ed. Engl., **1997**, *36*, 2450-2.

Synthesis, Structural Characterization, and Reactivity of Novel Zirconium (IV) Complexes Containing the Tropidinyl Ligand



Model Study - Process Overview



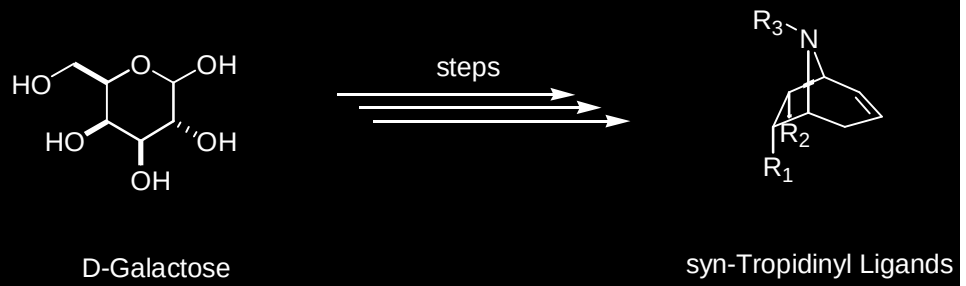
Model Study - Project Overview

- **Library Design**
  - Catalyst Hypothesis
  - Ligand Library Proposal
  - Computational Analysis
  - Ligand Library Design
  - Metallocene Proposal
  - Computational Analysis
  - Metallocene Library Design
- **Library Synthesis**
  - Ligand Synthesis
    - Methods Development
    - Optimization & Validation
    - HToS
  - Metallocene Synthesis
    - Methods Development
    - Optimization & Validation
    - HTomS

Model Study - Synthesis

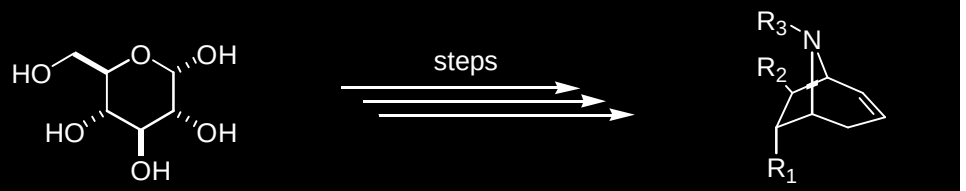
- **Synthesis**
  - Ligand Libraries from Chiral Building Blocks
  - Key Features:
    - Solid Phase Asymmetric Synthesis
    - Solution Phase Mods - Resin Covalent Capture
    - Tandem Grubbs Olefin Metathesis (ROM/RCM)
    - Auto-Purification

- **General Scheme**



D-Galactose

syn-Tropidinyl Ligands



α-D-Glucose

anti-Tropidinyl Ligands

Model Study - Screening

- **Polymerization & Primary Screen**
  - Construct Libraries of Polymerization Reactions
  - Variables: Complexes, Initiators, Monomers
  - Manipulate Reaction Conditions (P, T, Conc., EQ.)
  - Monitor Thermal Profile ($\Delta T/t$)
  - Monitor %Transmittance

Model Study - Screening

- **Sample Prep & Secondary Screen**
  - Crude Rxn Mixture Work Up
  - Analytical Daughter Plates (Solvent Manipulation)
  - 1H NMR Sample Prep (Continuous Flow Probe)
  - Filtration, Dilution, & Rapid GPC
  - Select Candidates for further Analysis

Model Study - Screening

- **Tertiary Screen & Advanced Properties**
  - Automated Thermal Analysis (DSC, TGA, TMA, etc.)
  - Advanced Properties Testing & Analysis
  - dB Correlation of Data
  - Optimization Libraries derived from Discovery Libraries
  - Scale-Up of Optimized Materials

Model Study - Analysis

- **Chemical Analyses**
  - Ligand Characterization
    - 1H NMR, FT-IR, LC-MS, Optical Rotation
  - Organometallic Complex Characterization
    - 1H NMR, FT-IR, LC-MS, Mass
  - Polymer Charaterization
    - 1H NMR (Tacticity), GPC (MW distribution)

Scylla Chemical's Strategy

- **Corporate Partnerships**
  - Technology, Compounds and Processes
  - Direct R&D Revenues, Licensing, Royalties
- **Government Grants co-sponsored with CP's**
  - NIST/ATP, NASA
  - SBIR, etc.
- **Internal R&D Operations**
  - 3D Libraries™, Resins & Polymers, Solid-Supported Catalysts, Catalysts, and Building Blocks.

Why ATP ?

- **Risk Analysis**
  - Technical Risks for Developing New Technologies
    - Nanoscale Systems, Screening & Analytical tools
  - Financial Risks
    - Systems Development Costs Could Exceed $100MM over 5-7 Years
- **Risk Assessments**
  - Too Costly for US Industry NOT to Automate CMS
    - European Industry has Embraced this Technology Paradigm
  - Market Gains
    - Accelerated Product Development, Increased Employment Opportunities, Technology Commercialization

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